of this arrangement it is possible to make the rotating disc travel horizontally above a large table in which are fixed a great number of pins, to the head of each of which is attached a bit of wool some centimetres in length, and thus forming many flags, which will show us the directions of the wind in each point traversed by the cyclone. In the centre of the table a hole is pierced communicating underneath with a very sensitive barometer, which will show us the variations of atmospheric pressure at the passage of the meteor (Fig. 8).

We set the rotating disc in rotation after having placed it above one of the extremities of the table; you see at once all the flags situated underneath indicate the directions of the wind. Those which form the centre of the whirlwind remain flat and rest inert on the table, their extremities directed one towards the other. They represent wonderfully well the central calm.

The flags surrounding the central calm form a circumference; they imply a wind forcing them all in a direction slightly centripetal, and ascending. In the following ranges the pieces of wool place themselves again along a circumference, but scarcely showing the centripetal direction, and not at all the ascending one; then the more distant the flags are from the centre, the more they inflect towards the table, and indicate the descending wind; at the exterior circuit the wool takes centrifugal directions; it is air which escapes from all sides on the borders of the cyclone.

Now, if we make the artificial cyclone travel horizontally, by moving the crane on its pivot, you will see that the central calm shows itself every instant at a new place, which is very easily observed by the aspect of the flags occupying the centre, which fall down suddenly and rest inert on the table. On the other hand the flags immediately adjacent raise themselves quickly, caught up by the tempest, and those which but recently were pointing in one direction, turn all at once in the opposite one, and make it possible to observe with all its sharpness the abrupt change of wind which takes place on leaving the central calm.

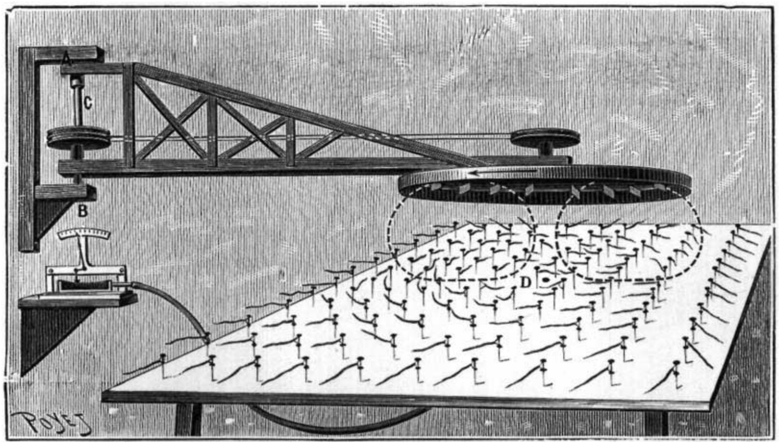

FIG. 8.—Artificial reproduction of cyclonic phenomena.

By making the cyclone travel with sufficient quickness, the flags permit us to take note of the dangerous and manageable sides of a cyclone, according as one looks at the semicircle in which the wind turns in the same direction as the movement of translation, or in the opposite one.

The variations of pressure are indicated by the passage of the cyclone above the hole made in the table, and communicating with the barometer; you see the needle falling little by little, indicating the minimum precisely at the moment when the centre of the cyclone passes above the hole, then rising slowly.

A thermometer sufficiently sensitive, placed in the centre of the cyclone, allows us to observe a rise of temperature.

In great cyclones, a ship on reaching the centre not only finds a general calm, but the sun or stars may be seen to shine through a great opening in the clouds; it is the eye of the storm.

In order to explain this fact, it suffices to remark that a cyclone is only in fact a water-spout of enormous diameter, in the immense sheath of which rages the storm of a descending movement, dragging down the hurricane and the clouds from the high regions to the level of the sea; but, as in the water-spout, the central nucleus remains free, and allows a clear sky to be seen.

The realisation of this eye of the storm succeeds equally well with steam or smoke by taking necessary precautions with the experiment.

Finally, as the centre of the cyclone is free of water vapour (at least in the visible form), whilst in the enveloping sheath storm and darkness reign, is it not evident that a hygrometer placed in this cloudy sheath will show a degree of moisture above that of the central nucleus?

To sum up—it may be seen that, however small the scale of the experiments in comparison to that which passes in nature, nevertheless these experiments reproduce with fidelity and with all the particularities of the great natural meteorological phenomenon.

The experiments which you have just seen will, I hope, suffice to show you how complete the experimental syntheses are, and how they represent the natural phenomena in the smallest details.

I will conclude by making the simple remark that meteorology gains in extent and certainly when we treat it as an experimental science.

A. CORNU.

IMMUNISATION AGAINST SERPENTS' VENOM, AND THE TREATMENT OF SNAKE-BITE WITH ANTIVENENE.[1]

II.

THE experiments now to be described were made with antivenene derived from a horse which had last received a dose of cobra venom estimated to be twenty times the minimum-lethal. On some previous occasions I have stated the results of observations on the antidotal value of the blood-serum of rabbits which had last received thirty and fifty times the minimum-lethal. The antivenene obtained from cats and white rats has also been examined. The special interest, however, is attached to antivenene derived from the horse, that it is more likely than any others to be used in the treatment of snake-bite in man.

The experiments were so planned as to obtain in different conditions of administration as exact a definition as possible of the antidotal power of the antivenene. In the meantime, four series of experiments have been undertaken on rabbits. In one series the venom was mixed outside of the body with the antivenene, and immediately thereafter the mixture was injected under the skin of the animal; in the second series the venom and antivenene were almost simultaneously injected into opposite sides of the body; in the third series the antivenene was injected some considerable time before the venom; and in the fourth series the venom was first injected, and thirty minutes afterwards the antivenene.

In the experiments of the *first series*, the doses of cobra venom administered were the minimum-lethal, one-and-a-half the minimum-lethal, twice, thrice, four times, five times, eight times, and ten times the minimum-lethal. In the case of each dose of venom, experiments were made with different quantities of antivenene, until the smallest quantity required to prevent death was discovered. In order to render it certain, in this and in the other series, that a lethal dose had been administered in the experiments with the so-called minimum-lethal, the minimum-lethal indicated by previous experiments was not used, but instead of it a slightly larger dose (·00025 instead of ·00024 gramme per kilogramme).

When this certainly lethal dose, capable of producing death in five or six hours, was mixed with the antivenene, and the mixture injected two minutes afterwards, under the skin, it was found that so small quantities were sufficient to prevent death as ·001 cc., ·0008 cc., ·0005 cc., and ·0004 cc. (1/1000, 1/1500, 1/2000, and 1/2500 of a cc.) for each kilogramme of the weight of animal; with ·0003 cc. (1/3333) per kilogramme, however, the animal died. The antivenene was therefore found to be so powerful as an antidote, in the conditions of these experiments, that even the 1/2500 part of a cubic centimetre, equivalent to about the one-hundred-and-fiftieth part of a minim, acted as an efficient antidote, while even with the one-two-thousandth part of a cubic centimetre not only was death prevented, but there was almost no symptom of poisoning produced. In the experiments of this series with one-and-a-half the minimum-lethal dose, recovery occurred when the doses of antivenene were ·32 cc., ·3 cc., ·28 cc., ·25 cc., and ·24 cc. per kilogramme; but ·23 cc. and ·2 cc. failed to prevent death. In the experiments with twice the minimum-lethal dose, recovery occurred when the doses of antivenene were ·5 cc., ·4 cc., and ·35 cc.; but ·3 cc. and ·2 cc. failed to prevent death. In the experiments with thrice the minimum-lethal dose, a dose capable of producing death in less than two hours, recovery occurred when the doses of antivenene were ·7 cc. and ·65 cc.; but death occurred with ·6 cc., ·55 cc., and 5 cc. With four times the minimum-lethal dose, recovery occurred with 1·5 cc., 1·3 cc., and 1·2 cc., and death with 1 cc. With five times the minimum-lethal dose, recovery occurred with 2·5 cc., 2·2 cc., 2 cc, 1·8 cc., and 1·5 cc.; but death with 1·3 cc. With eight times the minimum-lethal dose, recovery occurred with 2·6 cc. and 2·5 cc.; but death with 2·4 cc., 2·3 cc., and 2 cc. And even the enormous dose of ten times the minimum-lethal failed to produce death, or any important symptoms, when it had previously been mixed with 3·5 cc. and 3·4 cc. of antivenene for each kilogramme of animal; and it only succeeded in producing death, although not until the lapse of several hours, when the doses of antivenene were 3·3 cc., 3·2 cc., 3 cc., and 2·5 cc. per kilogramme.

---

[1] Continued from page 572.

These results show a remarkable, an almost directly proportional, accordance in the increment required in the dose of antivenene for each increment in the dose of venom. In the diagram the comparatively straight direction of the oblique line separating the fatal from the non-fatal experiments is noteworthy, considering that the conditions of the experiments, in regard both to the animals and the substances used, could never be absolutely the same. Indeed, from twice the minimum-lethal dose of venom upwards, the addition of little more than ·3 cc. per kilogramme represents the addition in the quantity of antivenene required for each addition of a minimum-lethal dose of venom. Apparently the antivenene is able in this proportion to prevent death from almost any lethal dose of venom, however large it may be.

These results are in marked contrast with those that occur when an antidote acts because of its physiological properties, and they alone suggest that the antidotism is rather the effect of a chemical than of a physiological reaction. The indications obtained with doses of twice the minimum-lethal and upwards cannot, however, be carried down to the minimum-lethal dose. The quantity of antivenene required to prevent death from this dose is much less than might have been anticipated when the results of experiments with larger doses are considered. Thus, it appears that while ·35 cc. of antivenene per kilogramme is required to prevent death from twice the minimum-lethal of venom, the minute quantity of the 1/2500th of a cc., or nearly 1000 times less (·0004 as compared with ·35 cc.), is sufficient to prevent death from a little more than the minimum-lethal dose of venom. It is apparent that this minute quantity of antivenene does not render inert the whole of the minimum-lethal dose. All that is required in order that the minimum-lethal dose should not produce death being that only a minute portion of it should be rendered inert; for, if this dose be the actual mininum-lethal, the rendering inert of any portion of it, however minute, will prevent the remainder from causing death.

In the *second series*, experiments with the antivenene of the horse have been completed only with one-and-a-half the minimum-lethal dose of venom. When this dose was injected into the subcutaneous tissues of one side of the body, and, immediately thereafter, a dose of antivenene into the subcutaneous tissues of the opposite side, it was found that antivenene in doses of 3 cc. and 3·3 cc. per kilogramme failed to prevent death, but that 3·5 cc. and 3·6 cc. per kilogramme were able to do so.

In the *third series*, experiments have been made with the minimum-lethal, one-and-a-half the minimum-lethal and twice the minimum-lethal dose of cobra venom. With the first of these doses, recovery occurred with ·5 cc., ·45 cc., and ·42 cc.; but death with ·4 cc., ·3 cc., and ·25 cc. of antivenene, administered thirty minutes before the venom. With one-and-a-half the minimum-lethal of venom, 2·9 cc. and 2·7 cc. of antivenene were able to prevent death; while 2·6 cc., 2·5 cc., 2·3 cc., and 2 cc. each failed in doing so. With twice the minimum-lethal dose of venom, recovery occurred when the doses of antivenene were 5 cc., 4·5 cc., and 4 cc.; but 3·9 cc., 3·8 cc., 3·5 cc., 2·5 cc., and 2 cc. were insufficient to prevent death.

In the *fourth series*, where the results give the truest indications of the antidotal value of antivenene in the actual treatment of snake-poisoning, it was found that recovery occurred in the experiments in which ·8 cc., ·7 cc., and ·65 cc. per kilogramme of antivenene was injected thirty minutes after an assuredly minimum-lethal dose (·00025 per kilo.) of venom; but that the antivenene was insufficient in quantity to prevent death when ·6 cc. or any smaller quantity was administered. In this series, further, it was found that 3·4 cc. and 3·2 cc. per kilogramme of antivenene were sufficient doses to prevent death after one-and-a-half the minimum-lethal dose of venom, but that 3 cc., 2·8 cc., and 2·5 cc. per kilogramme were insufficient. In a corresponding series of experiments made with the antivenene derived from rabbits which had last received thirty and fifty times the minimum-lethal dose of cobra venom, it was found that 5 cc. per kilogramme of this antivenene was the smallest dose by which death could be prevented in an animal which had received twice the minimum-lethal dose of venom thirty minutes previously.

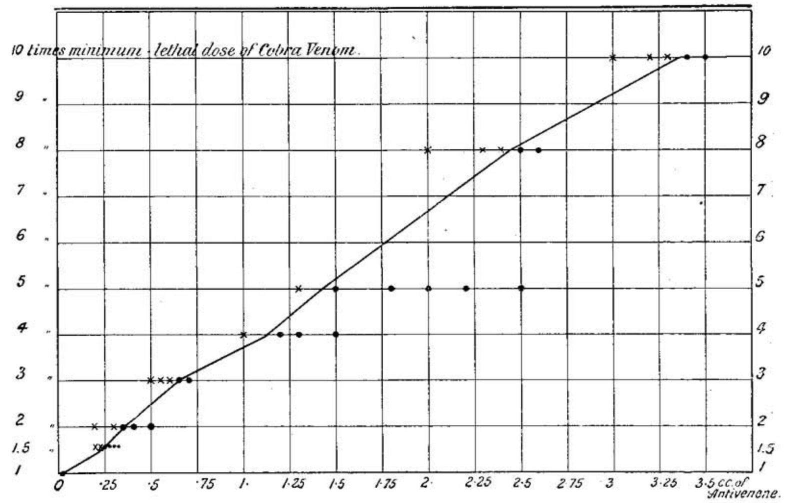

FIG. 2.

Attention is conspicuously drawn by these facts to the remarkable difference in the dose of antivenene which is required to prevent death when it is mixed with the venom before administration, as contrasted with the doses required when the two substances have not previously been mixed together. Restricting attention to the experiments in each series in which the dose of venom was the same—to the experiments with one-and-a-half the minimum-lethal dose, for instance—it appears that in order to prevent death, when this dose was mixed with antivenene before administration, only ·24 cc. of antivenene is required; whereas when both substances were injected simultaneously, but under the skin at different parts of the body, the required dose of antivenene is 3·5 cc.; when the antivenene was injected thirty minutes before the venom, it was 2·7 cc.; and when the venom was injected thirty minutes before the antivenene, it was 3·2 cc. per kilogramme.

It is impossible to consider the great difference between the dose of antivenene required when the two substances, though in each case simultaneously administered, are, in the one case, mixed together before injection, and in the other not so mixed, without again having the suggestion originated that the antidotism is the result of chemical and not of physiological reactions.

This suggestion receives a further support from the fact, observed in several experiments, that the longer before their administration the two substances were allowed to remain together after they had been mixed, the greater is the antidotal efficiency of the antivenene. Thus, while 1·3 cc. per kilogramme of antivenene, mixed with five times the minimum-lethal dose of venom, was followed by death when the two had been mixed together five and also ten minutes before administration, this mixture was, on the other hand, followed by recovery when the interval before the administration was extended to twenty minutes. In order to obtain uniform and comparable results in the first series of experiments, it was therefore found necessary to adhere, in all the experiments made with the larger doses of venom, to a time limitation of not more than ten minutes before the mixed substances were injected.

I have also administered cobra-antivenene thirty minutes after a dose one-twelfth larger than the minimum-lethal of the venoms, respectively, of the *Sepedon hæmachates*, the *Crotalus horridus*, and the Diamentina serpent; and the animals experimented on have recovered when the dose of cobra-antivenene was not smaller than 1·5 cc. per kilogramme. This successful result is all the more remarkable when the intensely destructive effects produced by even smaller doses of each, but especially of two, of these venoms is recollected.

The antivenene derived from rabbits which had been protected to the extent that they had last received fifteen times the minimum-lethal dose of the Diamentina venom has also been tested against the Diamentina venom itself. When the two were administered together, after having been mixed *in vitro*, this antivenene in a dose of ·05 (1/20) cc. per kilogramme was able successfully to antagonise slightly less than one-and-a-half the minimum-lethal dose of the venom; but ·025 (1/40) cc. per kilogramme failed to do so.

In the experiments which I have hitherto described, and, indeed, apparently in all others made in this new subject of serum therapeutics, protection has been produced, and the antidotal properties of the antitoxic blood-serum have been tested, by the subcutaneous, or, less frequently, by the intravenous injection of the venom or other toxic substance. No endeavour seems to have been made to discover how far the same effects, or what effects, may be produced by stomach administration.

Anticipating that results of an interesting nature might be obtained by this method of administration, I have adopted it for the introduction of both antivenene and venom into the body, and the results have even exceeded my anticipations.

The plan followed was the simple one of mixing the substances, previously dissolved in water, with a small quantity of milk, and allowing white rats, which had not received any food for several hours previously, to drink this milk. In the meantime, I will briefly describe only those experiments in which antivenene was thus administered, reserving, for a few minutes, a description of the results that were obtained when the venom itself was used.

The first experiments were made with the object of determining if, by repeating the process followed in the production of immunity, with the exceptions that the administrations were by the stomach and that antivenene was substituted for venom, an animal could be protected against the poisonous effects of venom. With this object, a white rat received on alternate days during several weeks, doses of antivenene, which were gradually increased from 1 to 10 cc. per kilogramme, and then, by subcutaneous injection, one-and-a-half the minimum-lethal doses of cobra venom; with the result that death was not produced. Other white rats received 10 cc. per kilogramme on each of four days, and on the fifth day 15 cc. per kilogramme of antivenene, and still recovery took place when one-and-a-half and one-and-three-quarters the minimum-lethal dose of venom was injected under the skin. To other white rats, 10 cc. and 15 cc. of antivenene were given by the stomach, on two successive days, and on the second day, one-and-a-half the minimum-lethal dose of venom, and the result also was that death was prevented. It was thus suggested that a single administration of antivenene might be as efficacious as a succession of administrations; and accordingly, the antidotal efficiency of single doses of 7 and of 10 cc. per kilogramme was tested, in some instances three hours, in others two days, and in others three days before one-and-a-half the minimum-lethal dose of venom was subcutaneously injected; and in all cases the animals recovered. When, however, 5 cc. per kilogramme of antivenene was thus administered three hours before, and 10 cc. per kilogramme three days before, one-and-a half the minimum-lethal dose of venom, the animals died.

The experiments have not as yet been carried further, but I hope to continue them so that the limits of the antidotal power of the antivenene, and the duration of the protection after single doses of antivenene, may be defined. Enough has, however, been done to prove that the stomach administration of antivenene, equally with its subcutaneous administration, confers protection against lethal doses of serpents' venom, and to justify the use of antivenene by the former and more convenient method for the purpose of securing protection for, at least, a period of several days after a single administration of the protecting antidote.

The facts hitherto narrated are sufficient to establish that the protection acquired by animals as a result of the administration of venom is not chiefly, or even to any important degree, caused by the venom having produced a tolerance by accustoming the body, as it has been expressed, to the presence of the venom—although a certain degree of this protection may possibly be due to such accustoming—but rather to the presence in the body, as a result of the introduction into it of venom, of a definite substance having antivenomous qualities. Notwithstanding the powerful protective and antidotal action of this substance (antivenene) against serpents' venom, it is instructive to find that it is itself almost devoid of any physiological action, for even very large quantities may be injected under the skin without producing any other physiological reaction than a moderate degree of irritation in the neighbourhood of the injection. How then are we to explain the operation of this physiologically inert substance in protecting an animal against even fifty times the minimum-lethal dose of venom, or by a single administration of it, in saving an animal from death after there has been introduced into its body more than twice the quantity of venom that is required to kill it? When an answer has been attempted to be given to this question in discussions in the wider field of the serum therapeutics which deals with the toxines of diseases, the answer has been found either in the destructive power of phagocytes upon microbes and their toxines, or in the theory that the toxine elaborates from the blood the antidotal antitoxine, which, whether thus originated or separately introduced into the body, confers upon the body a resisting power which enables it to oppose successfully the injurious action of the toxines.

These answers cannot solve the problem in so far as snake venom is concerned. Phagocytosis cannot, of course, operate *in vitro* in solutions which are free from organised structures. Even when solutions of venom and antivenene, mixed together *in vitro*, have been inserted into the body, it is incredible that the increase in the quantity of antivenene by the 1/500th part of a cubic centimetre could cause such an increased proliferation of leucocytes as to prevent a lethal dose of venom from producing death, whereas a dose only the 1/500th part of a cubic centimetre smaller would be unable to do so. Further, there is no observable increase of leucocytes when much more than these infinitesimal quantities of antivenene have been administered to an animal.

In view of many of the facts that have to-night been stated, the "resistance of tissues" theory is also untenable. It is opposed, for instance, by the fact that so great a quantity of antivenene as ·42 cc., or nearly ½ of a cubic centimetre per kilogramme is required to prevent death when given thirty minutes before a lethal dose of venom, whereas, for the same dose of venom, only ·0004 cc. or the 1/2500th part of a cubic centimetre, or nearly the 1/000th part of the former dose is sufficient, when it is mixed with the venom before administration, and in circumstances, therefore, which are much less favourable for the production by the antivenene of this supposed increase in the resistance of the tissues.

As I have already pointed out, however, a chemical theory, implying a reaction between antivenene and venom, which results in a neutralisation of the toxic activities of the venom, is entirely compatible with the observed facts.

The experiments which I have described to-night indicate that, with some limitations in the largest quantities, the greater the quantity of venom that has been introduced into the body in the process of producing protection, the greater is the antivenomous power of the blood-serum, and therefore the larger is the production of the antivenene. While not an actual proof, this circumstance is at the same time in harmony with the supposition that the antivenene may actually be a constituent of the venom itself. The difficulties encountered in the separation by chemical methods of the several constituents of venom are so great, that it is not probable that the only proof or disproof of this supposition will soon be obtained by chemical analysis. Some physiological experiments which I have made seem, however, to go a long way in supplying the demonstration, which in the meantime has not been obtained from chemistry.

With the object of determining, in the first place, if the still disputed statement is correct that serpents' venom is inert, or nearly so, when introduced into the stomach of an animal, cobra venom was administered, in a series of gradually increasing doses, to a cat, until finally it had received a single dose eighty times larger than the minimum-lethal; and to each of six white rats, single doses corresponding to 10, 20, 40, 300, 600, and 1000 times the minimum-lethal, if given by subcutaneous injection. Although no poisonous symptoms were produced in the animals by even the largest of these enormous quantities, it was found that the cat had so far been protected, that it could afterwards receive, by subcutaneous injection, one-and-a-half the minimum-lethal dose of cobra venom, without any other injury than some localised irritation at the seat of injection; and that the white rat, into whose stomach 1000 times the minimum-lethal dose had been introduced by one administration, survived perfectly, when seven days afterwards slightly more than the minimum-lethal dose of venom was injected under the skin.

It was also found that the blood-serum of the cat was definitely antivenomous, and the curious further fact was ascertained that her progeny had acquired protection through the milk supplied by the protected mother, thus supplying a scientific foundation for a half-admitted conviction, expressed by Wendell Holmes throughout his "Romance of Destiny," in regard to the heroine Elsie Venner.

These significant facts have been extended in a number of other experiments on white rats. In one group of experiments, each animal received, by stomach administration, 500 times the minimum-lethal, if given subcutaneously; and, as before, no toxic symptoms were observed. On the day following this administration, three of the animals received subcutaneously one-and-a-half the minimum lethal dose of the same cobra venom, and they all recovered. In one of the other three animals, however, death was caused by this dose, when it was injected only three hours after the stomach administration; in a second, when this dose was injected two days after the stomach administration; and in the third, when nearly twice the minimum-lethal was injected twenty-four hours after the stomach administration.

In a second group of experiments, a dose of cobra venom equivalent to 1000 times the minimum-lethal by subcutaneous injection was introduced into the stomach. On several occasions in which this had been done, an injection under the skin of one-and-a-half the minimum-lethal dose of venom made, in some experiments, two days, and in others three days afterwards, resulted in the recovery of the animals. As was anticipated, this large quantity introduced into the stomach, conferred immunity against only certain lethal doses of venom, and, for each lethal dose capable of being rendered innocuous, only within certain definable intervals of time.

The extraordinary result was thus obtained that serpents' venom introduced into the stomach in large quantity—in a quantity, which if injected under the skin would be sufficient to kill 1000 animals of the same species and weight—while it failed to produce any definite symptoms of poisoning, nevertheless produced complete protection against the lethal effect of doses of venom more than sufficient to kill the animals. There is a probable significance, further, in the general resemblance between the results of these experiments and those already described in which antivenene, and not venom, was introduced into the stomach. The bearing of these facts is obvious upon discussions relating to the production of immunisation against the toxines of diseases and to the origin of the antidotal qualities of the blood-serum used in their treatment. It is difficult to account for them otherwise than by supposing that the venom while in the stomach had been subjected to a process of analysis, by which the constituents which are poisonous had failed to be absorbed into the blood, or had been destroyed in the stomach or upper part of the alimentary canal, while the constituent or constituents which are antivenomous, or rather antidotal, had passed into the blood, in sufficient quantity to protect the animals against otherwise lethal administrations of venom. I confidently anticipate that this natural process of analysis will, by-and-by, be successfully repeated outside of the body by chemical methods.

It is further to be observed that by stomach administrations a degree of protection was acquired in a few hours against lethal doses, such as cannot be attained until after the lapse of several weeks by the method of injecting under the skin a succession of gradually increasing doses of venom. In circumstances, which are no doubt exceptional, the application of this method may therefore acquire some practical value.

Early this evening, I had occasion to point out that the leading facts connected with immunisation or protection, now being advanced as scientific novelties, had apparently been ascertained and practically applied for centuries by savage and uncultured tribes and sects in various parts of the world. In regard to the results I have last described, also, I discover that I have been anticipated by a long-existing and even now prevailing practice of unlearned savages. I have found in the *Lancet* of 1886, an interesting note by Mr. Alford Bolton, containing the following: "The most deadly snakes here are the puff-adders, the yellow cobra capellas, the horn-snakes, and the night-adders. Whilst frequently hearing of horses and cattle rapidly succumbing to the bites of these snakes, it appeared strange that the natives themselves, who mostly ramble about the Veldt almost naked, seldom or never appeared to suffer any further inconvenience from the bites of poisonous snakes than would be usual from any accident which would cause a local inflammation; and, on close inquiry, I found that the natives in Bushmanland, Namaqualand, Dumaraland, and the Kalakari, are in the habit of extracting the poison-gland from the snake immediately it is killed, squeezing it into their mouths, and drinking the secretion, and that they thereby appear to acquire absolute immunity from the effects of snake-bites." He proceeds to describe the native treatment of snake-bite, and then adds: "Having a month ago seen a native named Snellsteve, who is a snake-poison drinker and collector, put his hand into a box containing two yellow cobras, and several horn- and night-adders, in doing which he was severely bitten, and has never since suffered anything more than a little pain, such as might be caused by any trivial mishap, I feel I can no longer refuse to believe in the efficacy of the snake virus itself as a remedy against snake-poison." Among several communications which I have recently received on the subject, is one from Dr. Knobel, of Pretoria, who writes that when a boy he came into frequent association with a Bushman shepherd, who informed him that he had for years been in the habit of swallowing small quantities of the dried venom-glands of serpents, and he averred that by doing so he obtained protection against serpents' bites, for he had often been bitten without any other ill-effect than that an irritable wound was produced. He stated that the swallowed venom of the cobra produced greater protection than the venoms of less poisonous serpents; and that not only was this benefit produced by the swallowing of venom, but that there was also produced an exciting intoxication, differing from that of Indian hemp in so far that the venom always produced the same degree of intoxication with a definite quantity, however frequently it was taken, while the effects of the Indian hemp were gradually lessened by repetition. Another correspondent, Dr. Laurence, of Cape Colony, writes that a Kaffir boy, "aged about twenty-five years, frequently brings me for sale snakes of all kinds. . . . I have frequently seen this boy take hold of some most deadly snakes, especially the well-known puff-adder, which he will allow to bite him with impunity. Yesterday, I obtained from him what he states as the reason why the poison did not harm him. When a little boy, while walking in the Veldt, a puff-adder fastened on his leg. He shook it off, calling to his father, who a few minutes after killed the puff-adder and removed the poison glands. He then made small paper pellets and dipped them in the poison, and administered one occasionally to the boy, who stated that that cured him. He expressed his willingness to let any snake bite him." Several other letters I have received describe similar events, and also confirm the statement of Dr. Knobel, that serpents' venom produces intoxicating effects in man, evidences of which have been observed in many of the experiments made by me on the lower animals.

The results of the experiments in which the venom was introduced into the stomach, probably also afford an explanation of the protection enjoyed by certain snake-charmers, as well as by other individuals who claim to be protected, whether members of special sects or not; for although inoculation of the venom is apparently sometimes practised by them, and protection is no doubt assisted and maintained by the bites, which with impunity they frequently receive, they are known also to swallow the venom or the dried poison-glands containing it.

These experiments also seem to throw a new light upon the clearly established protection possessed by venomous serpents against their own venom. They suggested the importance of determining if the blood-serum of venomous serpents contains, as does that of artificially protected animals, an actual substance possessing antivenomous properties.

In order to arrive at some definite conclusions on this subject, I last year obtained from India several living specimens of the Hamadryad (*Ophiophagus elaps*), a serpent of greater size and more aggressive disposition than the cobra, and reputed to be as deadly as it. From the blood of several of these serpents a serum was separated, which when dried gave a product having the same physical characters as the antivenene from artificially protected animals. It was tested against cobra venom, both when mixed with rather more than a minimum-lethal dose, and also when injected thirty minutes after this lethal dose of cobra venom. In the former case, ·25 cc. per kilogramme of this natural antivenene prevented death; and, indeed, so perfectly antagonised this certainly lethal dose that no decided symptoms of poisoning were manifested. In the latter case, 5 cc. per kilogramme was found to be a sufficient quantity to prevent death. I hope by-and-by to extend these observations by testing the antidotal power of this serum against the venom of the actual Hamadryads from whose blood it had been separated.

A determination of this kind has, however, been made with the blood-serum and venom of the Australian black snake (*Pseudechis porphyriacus*), a deadly serpent whose bite produces intense destructive changes, not only at the place where it has been inflicted, but also in the blood and in many of the organs of the body. When the blood-serum and the venom of this serpent were mixed together outside of the body, and then injected under the skin of a rabbit, it was found that half a cubic centimetre per kilogramme of the blood-serum was sufficient to prevent death from rather more than the minimum-lethal dose of venom.

Notwithstanding the obliging co-operation of the India Office, I have not yet succeeded in obtaining the blood-serum of the cobra, but it may safely be anticipated that it also will be found to possess antivenomous properties.

It has thus been shown that venomous serpents themselves possess a definite substance in the blood-serum which is capable of protecting them against their own venom, and the venom of other serpents. The results of the experiments made by stomach administration of venom, supply at the same time an explanation of one, at least, of the methods by which this substance is introduced into the blood. This natural antivenene, however, is apparently not so powerfully antidotal as the antivenene obtained by the process of artificial protection.

The foregoing statements, although referring mainly to observations on the lower animals, have, probably in every particular, a very direct bearing upon both the prophylaxis and treatment of snake-poisoning in man.

Some little consideration of the details of the application of the antivenene and the employment of auxiliary measures may, however, be serviceable; and, equally of practical service, some consideration of the probable limitations to the capacity of antivenene as an antidote.

In the meantime, I cannot adduce any actual experience of its use in human beings, as although a considerable quantity, both in the liquid and dry state, was last summer sent to India, and a smaller quantity to Africa, no opportunity for using it as an antidote has as yet occurred in the districts to which it had been sent.

But, first, let me say in regard to the altogether unsatisfactory experience of the use of medicines, ordinarily so-called, that I am not prepared to take the extreme position that no good can be done by their employment. While the evidence shows that no one of the very large number of those that have been recommended as antidotes is able, in any conditions of administration, to prevent death after the reception of even the smallest lethal dose of venom, it still may be that, by the physiological effects which they produce, they may assist any efficient antidote, such as antivenene, in preventing death; and also, by prolonging life, increase the opportunity for a more thorough use of this antidote. In this category I would especially place medicines which increase excretion, such as diaphoritics and diuretics; many of the rapidly acting stimulants of the circulation, such as alcohol and the old snake remedy, ammonia; and stimulants of respiration, such as atropine and strychnine, the latter of which is enthusiastically championed by Dr. A. Mueller, of Sydney. And not only medicines, but also any measures that are available for these purposes, including artificial respiration, so distinctly indicated as a probably valuable therapeutical application in snake-bite by Fayrer and Brunton, which, though shown by the Indian Snake Commission to be incapable of preventing death when alone trusted to, was also shown to possess the valuable auxiliary power of prolonging life.

The first measure, however, that is usually and properly taken in the treatment of snake-bite, is to restrict, as far as possible, the absorption of the venom into the blood-vessels, from the place into which it has been injected by the poison-fangs, by separating this part from the more central parts of the body by a tight ligature. The efficiency of this measure, preventive rather than curative, is fortunately aided by the circumstance that snake-bites are most usually inflicted at parts to which a ligature can conveniently be applied; for in fifty-four cases collected by Wall, the part in nearly 89 per cent. of the cases was on the arms or legs. The ligature having been applied, whenever it is possible to do so, the next measure to adopt is to open up with a knife, to a considerable depth, the minute though deep punctures made by the fangs, and then to apply suction to the wound. Justification is found for this procedure in the fact, demonstrated by experiment, that notwithstanding the rapidity with which venom may be absorbed, a portion of it still remains for a considerable time in the tissues immediately surrounding the wound. This has been clearly demonstrated by both Kaufmann and Wall. The suction may be produced by the mouth, and in the absence of more effective apparatus this ready method would be serviceable, while it is attended with danger to the operator only in the infrequent occurrence of fissures or abrasions of the mouth. It is, however, more effectively and without any risk accomplished by a suction pump, such as the most useful pump invented by Mr. Andrew Smith, of Cape Colony, which I now show.

These steps having been taken, antivenene should be injected into the tissues at and near the wound and, also, under the skin above the ligature, and the ligature should not be removed until at least half an hour after a sufficient quantity of antivenene has been injected under the skin above it.

But the important question has yet to be answered, What is a sufficient quantity? The whole tenour of my remarks to-night has been to show how necessary it is to bear in mind that there is a definite relationship between the dose of venom received and the dose of antivenene required to antagonise it, and that this relationship also varies with the conditions of the administration of the antivenene, and, especially, with the interval of time that elapses between the reception of the venom and the administration of the antivenene.

In snake-bite in man it is impossible to estimate the dose of venom which has been injected, for the nature of the symptoms in the patient cannot give the information even approximately. In searching for a solution of this problem, several facts may be taken into consideration from which assistance may be obtained. And, firstly, what is the probable quantity of venom that a serpent injects into a wound? Some data for answering this question have, very kindly, been obtained for me by Brigade-Surgeon Lieut.-Colonel Cunningham, of Calcutta. Taking nine adult cobras, healthy and vigorous, he collected from each the venom ejected at a single bite, dried and weighed each collection separately, and sent me the weights. They are as follows;—

(1) 0·726 gramme.
(2) 0·262 ,,
(3) 0·115 ,,
(4) 0·144 ,,
(5) 0·132 ,,
(6) 0·113 gramme.
(7) 0·239 ,,
(8) 0·306 ,,
(9) 0·253 ,,

The total venoms yield an average of 0·255 gramme for each bite; but, if the exceptionally large quantity stated in the first figure be excluded, the average for the remaining eight becomes ·195 gramme. It must also be considered that these quantities were obtained in the most favourable conditions for securing the total quantity ejected at a single bite, whereas in actual practice the conditions are less favourable for the insertion of the total available venom into the tissues of the victim.

Reverting now to determinations of the minimum-lethal dose for the lower animals, we find that if the minimum-lethal dose for the cat be adopted as being the same as that for man, the total quantity of dry cobra-venom required to kill a man of ten stones weight would be ·317 gramme, which is considerably more than the quantity, judging from the above averages, that a cobra is usually able to eject during a single bite. It would therefore appear necessary to assume that the minimum-lethal dose per kilogramme for man is smaller than for a cat; but, as it is probably greater than for a rabbit, we may for convenience assume that it is twice that dose. In this case, the smallest quantity required to produce death in a man of ten stones would be about ·0317 gramme, which, however, seems to be considerably less than the quantity which a fresh cobra has at its disposal. Applying now the facts that have been stated in the series of experiments where the smallest quantity of antivenene required to prevent death when injected thirty minutes after twice the minimum-lethal dose was determined, it will be recollected that that quantity is 5 cc. per kilogramme of animal. Taking this as a basis for the dose of antivenene, in order to prevent death in man from the estimated minimum-lethal dose of cobra-venom, so considerable a quantity as 330 cc., or about 11½ ounces, of antivenene would be required, if the antivenene be injected not much longer than thirty minutes after the bite had been inflicted. This, though a large, is by no means an impossible dose, and it could, without much inconvenience, be introduced under the skin at several parts of the body.

On the other hand, the estimate which I have adopted of the minimum-lethal dose for man may be too high a one, and if it should prove to be nearer that for the rabbit, then the quantity of antivenene required to prevent death, if administered half an hour after the snake-bite, would be reduced to about four ounces. It is also to be recollected that if dry antivenene be used, it may be dissolved in a much smaller quantity of liquid than is required to restore it to its original bulk.

As to the probability, in a fatal snake-bite, of the quantity of venom received by the victim being only about, and not much in excess of, the minimum-lethal dose, it would appear that, in many cases, even so large a dose is not introduced; for general experience indicates that the majority of persons who are bitten actually recover, whatever treatment is adopted. Sir Joseph Fayrer also shows, in his classical "Thanatophidia," that in 64 per cent. of fatal cases of snake-bite in India, the victims survived the infliction of the bite for periods of from three to twenty-four hours; and this duration of life implies that the dose of venom received, could not have been much greater than the minimum-lethal.

It must be admitted, however, that even for the minimum-lethal dose of venom, the quantity of antivenene required to prevent death in man is probably inconveniently large, especially if, in the treatment, reliance is placed solely upon the administration of antivenene, to the exclusion of all or several of the auxiliary measures to which I have referred. It is desirable, also, that the antivenene treatment should be a practical one, not only for doses of venom which do not much exceed the minimum-lethal, but also for the considerably larger doses that are occasionally introduced in snake-bite.

To attain this object, further work is required in order that there may be obtained an antivenene even more powerful than that whose antidotal capabilities I have described.

I am not sanguine that this will be accomplished by carrying to a higher degree the process of artificial protection in animals. A comparison of the antivenene of rabbits which had last received thirty times the minimum-lethal dose of cobra venom with that of other rabbits which had last received fifty times that dose, has shown that the latter has but little antidotal advantage over the former, and has suggested that, in the process of artificial protection, the saturation point of the blood for antivenene is reached before the possible maximum non-fatal dose of venom has been administered.

I would anticipate with more hope the results of endeavours to separate the true antivenomous principles from the inert constituents of the blood-serum with which they are mixed; and although the required chemical manipulations are attended with many difficulties, some success has already been obtained in effecting this separation.

In the foregoing remarks, it has, however, been shown that even with the antivenene whose properties have been described, human life may be saved in a considerable, if not in a large, proportion of the cases of snake-bite, which would otherwise terminate in death. The attainment of this result is a satisfactory one; for the mortality from snake-bite is large, and is not restricted to the 20,000 deaths which annually occur in India, but includes additional thousands in all the tropical and sub-tropical regions of the world.

THOMAS R. FRASER.

UNIVERSITY AND EDUCATIONAL INTELLIGENCE.

The Drapers' Company have voted £50 to Mr. Percy Williams, a student at University College, London, towards paying his expenses of post-graduate study. Mr. Williams was placed first in honours in his chosen faculty at the B.Sc. Examination of last year in connection with the London University.

It is stated that the total subscriptions promised for the new building fund of the University College of South Wales and Monmouthshire amounts to over £16,000. The Treasury has authorised the payment of £10,000 to the building fund, this being half the sum promised by her Majesty's Treasury on condition that £20,000 was collected in South Wales and Monmouthshire by July next.

The University of Utrecht will celebrate its "260th lustrum" during the month of June next. The occasion will be rendered specially interesting by the *fêtes* which will be given by the students, and which will include their traditional masquerade and an elaborate old world tournament. It is expected that the ancient city will be visited by numerous strangers during the commemoration.

A municipal school of science and art was opened at Bideford on Wednesday, April 15. For some time past instruction in science and art has been given with great difficulty in ill-fitted and unsuitable rooms. The cost of the new school will be about £3000, towards which the County Council have contributed £500 (with a promise of £75 towards science apparatus), the Science and Art Department will grant £650, and a penny rate has yielded £700.

We learn from the *Athenæum* that the Committee of the Aberdeen University Council, which has been considering measures for the extension and better endowment of the university, has issued a report enumerating, "among its more pressing wants," the enlargement of the library, laboratory, and museums, a botanic garden, residential halls for both sexes, seven new professorships, and fifteen lectureships. The report also advises the establishment of an Aberdeen University Association, on the model of the Edinburgh Association.

On Tuesday, April 14, the Right Hon. Sir William Hart-Dyke visited Bath and opened the northern wing of the new municipal buildings which has been appropriated to the purpose of technical schools. The building, which cost £30,000, was commenced about eighteen months ago, and comprises four floors. The basement consists of workshops and mechanical and electrical laboratories; the ground-floor includes large and small lecture-rooms, and accommodation for the library and lecturers' and director's rooms. The first-floor constitutes the school of art, while the second-floor contains a domestic department and chemical and physical laboratories.

A Confererce on Secondary Education was opened on Tuesday in the Senate House, Cambridge, under the presidency of the Vice-Chancellor of the University. A resolution generally approving of the scheme set forth in the report of the Royal Commission on Secondary Education, and expressing a hope that legislative measures in accordance with that report would be passed, was carried by 128 to 41 votes. A resolution approving the establishment of local authorities for secondary education was also carried, after considerable discussion. Resolutions were subsequently agreed to in favour of the establishment of a separate central authority for secondary education, and of the preservation of the freedom, variety, and elasticity which have hitherto characterised secondary education in England.

The following are among recent appointments abroad:—Dr. Paul Czermak, *privat-docent* in Physics in Gratz University, to be extraordinary professor; Mr. James Edwin Lough to be